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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/872,836	06/01/2001	Shikha P. Barman	08191-018001	3677
26161 7590 01/24/2008 FISH & RICHARDSON PC P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER SAJJADI, FEREDOUN GHOTB	
			ART UNIT 1633	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/872,836

Applicant(s)

BARMAN ET AL.

Examiner

Fereydoun G. Sajjadi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 November 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16, 21-29, 31-34 and 37 is/are pending in the application.
- 4a) Of the above claim(s) 5 and 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-16, 21-24, 26-29, 31-34 and 37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Status

Applicant's response of August 22, 2007, to the non-final action dated February 22, 2007 and the amendment filed November 20, 2007, have been entered. No claims were amended, canceled or newly added. Claims 1-16, 21-29, 31-34, and 37 are currently pending in the application. Claims 5 and 25 remain withdrawn from consideration, without traverse. Claims 1-4, 6-16, 21-24, 26-29, 31-34 and 37 are under current examination.

Response to Claim Rejections – 35 USC § 103(a)

Claims 1-4, 6-16, 29, 32-34, and 37, stand rejected under 35 U.S.C. 103(a) as being unpatentable over Papahadjopoulos *et al.* taken with Rolland (U.S. Patent No.: 6,040,295; of record), and further in view of Lunsford (U.S. Patent Publication No.: 2002/0182258; of record).

Claims 1-4, 6, 7, 9-16, 26, 29, 32-34, and 37, stand rejected under 35 U.S.C. 103(a) as being unpatentable over Papahadjopoulos *et al.* taken with Rolland, and further in view of Mathiowitz (U.S. Patent No.: 6,677,313; of record). The rejections set forth pp. 5-10 of the office action dated October 6, 2005; and pp. 3-5 of the previous office action dated February 22, 2007 are maintained for claims 1-4, 6-16, 26, 29, 32-34, and 37 for reasons of record.

Applicants traverse the rejection and argue that the skilled person would not have had any reason to entrap a lipid:nucleic acid:PEG-DSPE complex disclosed in Papahadjopoulos within a microparticle described in Lunsford or Mathiowitz. Further arguing, the reason for including a hydrophilic polymer (e.g., PEG-DSPE) in the lipid:nucleic acid complexes of Papahadjopoulos was to prevent aggregation of the complexes, and the need to prevent lipid:nucleic acid complex aggregation would clearly be absent if a lipid:nucleic acid complex of Papahadjopoulos were to be entrapped in a microparticle of Lunsford or Mathiowitz. Furthermore, even if one were to attempt to entrap selected components (e.g., a cationic lipid and a nucleic acid) of a Papahadjopoulos composition in a microparticle of Lunsford or Mathiowitz, the skilled person would have had no reason to also include a hydrophilic polymer (e.g., PEG-DSPE) in such a

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composition. Applicants' arguments have been fully considered, but are not found to be persuasive.

In response, it should be noted that the primary reference is that of Papahadjopoulos *et al.*, disclosing lipidic microparticles linked to targeting moieties (Abstract), prepared by contacting a nucleic acid with an organic polycation and an amphiphilic cationic lipid and then combining the complex thus formed with a hydrophilic polymer, that may be PEG-DSPE (columns 3 and 4 bridging). Papahadjopoulos *et al.* clearly teach that "the lipids need not be provided as a liposome." (column 10). They further state: "It is also recognized that after complexation, the lipid:nucleic acid complex may no longer exist as a true vesicle and therefore is not generally regarded as a liposome." (column 10). As such, the microparticles of Papahadjopoulos *et al.* are not encapsulated in a liposome and do not comprise a cell.

Lunsford claims (section 21, claim 1), a microparticle comprising a polymeric matrix, a lipid and a nucleic acid molecule that is not encapsulated. Neither Papahadjopoulos, nor Lunsford require the encapsulation method described by Mathiowitz. The applicant's are reminded that for the purpose of combining references under 35 U.S.C. 103(a), the test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Further, those references need not explicitly suggest combining teachings, much less specific references. *In re Nilssen*, 7 USPQ2d 1500 (Fed. Cir. 1988). The reference to Mathiowitz was used for an entirely different purpose and to address a separate limitation. Mathiowitz was not used to require the products of Papahadjopoulos, or Lunsford be encapsulated. As previously stated, the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). Moreover, the reference of Mathiowitz is not required for the rejection of claims 1-4, 6-16, 29, 32-34, and 37. Just as we look to a chemical and its properties when we examine the obviousness of a composition of matter claim, it is this

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invention as a whole, and not some part of it, which must be obvious under 35 U.S.C.103.” *In re Antonie*, 559 F.2d 618, 620, 195 USPQ 6,8 (CCPA 1977).

Applicants should additionally note that in the instant case, the teachings of Mathiowitz et al. need not be applied under the strict application of the TSM (teaching, suggestion or motivation) test. While the TSM test of obviousness has been applied to provide reasoning for substituting known elements, such substitution amounts to simple substitution of one known element for another to obtain predictable results. Accordingly, there is no reason not to include or substitute a hydrophilic polymer (e.g., PEG-DSPE) in the microparticle compositions. Applicants should further note that the *KSR* case forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR International Co. v. Teleflex Inc.*, 550 U.S.-, 82USPQ2d 1385 (2007).

Therefore, the rejection of claims 1-4, 6-16, 26, 29, 32-34, and 37 is maintained for reasons of record and the foregoing discussion.

Claims 21-24, 26-28, and 31 stand rejected under 35 USC 103(a) as being unpatentable over Lunsford (U.S. Patent Publication No.: 2002/0182258), in view of Papahadjopoulos *et al.* (U.S. Patent No. 6,803,053). The rejection set forth pp. 5-7 of the previous office action dated February 22, 2007 is maintained for reasons of record.

Applicants traverse the rejection, arguing Lunsford does not describe or suggest including in a microparticle a lipid (such as PEG-DSPE) having a pKa of less than about 2.5. Applicants additionally argue that Papahadjopoulos describes the inclusion of PEG-DSPE in lipid: nucleic acid complexes as a means to prevent aggregation of the complexes and thereby enhance their shelf life, and this function would be irrelevant in the microparticles of Lunsford. As a result, the skilled person would have had no reason to include a lipid such as PEG-DSPE in a microparticle of Lunsford. Applicants’ arguments have been fully considered, but are not found to be persuasive.

Lunsford et al. disclose a preparation of microparticles for delivery of nucleic acids comprising a polymeric matrix, a nucleic acid expression vector, and a lipid, wherein the microparticles have a diameter less than about 100 microns (Abstract and Title). Lunsford et al. state that the lipid may be a cationic lipid or a phospholipid, thus providing the motivation to

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incorporate any cationic lipid or phospholipids in their polymeric matrix to form a microparticle. The instant claims do not stand rejected for anticipation by Lunsford et al. Thus, there is no requirement for Lunsford et al. to specifically disclose PEG-DSPE as the phospholipid to be utilized in their microparticle composition, in an obviousness rejection. Thus, at the time of the instant invention it would have been *prima facie* obvious for one of ordinary skill in the art to include PEG-DSPE disclosed by Papahadjopoulos *et al.* in the microparticle of Lunsford et al., with a reasonable expectation of success, to produce the microparticle of the instantly claimed invention. The pKa associated with PEG-DSPE is a property inherently possessed by the lipid and is immaterial to the patentability of the claimed invention. One of ordinary skill in the art would have been motivated to utilize PEG-DSPE as a lipid in the polymeric matrix composition of Lunsford et al., because the inclusion of cationic and phospholipids was expressly provided for by Lunsford et al.

Therefore, the rejection of claims 21-24, 26-28, and 31 is maintained for reasons of record and the foregoing discussion.

Conclusion

No claims are allowed.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR § 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is (571) 272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Fereydoun G. Sajjadi, Ph.D.
Examiner, AU 1633



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